

D J

carboxyalkylation is a carboxymethylation. The term "derivatizing" and related terms (e.g. derivatives, derivatized, derivatization, etc) refer to the conventional sense of functionalization at the reactive sites of the composition. Further according to this method, the reduced polysaccharide can be a reduced dextran. The derivatized, reduced polysaccharide can be isolated as the sodium salt and does not contain an infrared absorption peak in the region of 1650-1800 cm⁻¹. In one aspect of the method, producing the derivatized reduced polysaccharide is achieved at a temperature of less than approximately 50°C. In another aspect of the method, producing the derivatized reduced polysaccharide is achieved at a temperature of less than approximately 40°C. In a further aspect of the method, the iron oxide is superparamagnetic.

MARKED UP PARAGRAPHS

In the Specification:

Replacement Page 1, paragraph 1, Background.

Since the invention of magnetic resonance imaging (MRI), a parallel technology of injectable chemicals called contrast agents has developed. Contrast agents play an important role in the practice of medicine in that they help produce more useful MRI images for diagnostic purposes. In particular, two classes of imaging agents have been developed and adopted in clinical practice. These are: low molecular weight gadolinium complexes such as Magnavist®; and colloidal iron oxides. Neither of these two types of agents is ideal. Problems encountered with these agents are shown in Table 1, and include: expense of components; inefficiency of synthesis; loss of coating if

sterilized by autoclaving; narrow range of organ uptake for purposes of imaging; side-effects [~~at doses in vast excess, for example, 100 mg/kg body weight~~]; restriction of use to either first pass or equilibrium dosing; and others that are described herein. Agents that overcome these problems, and that combine the properties of these two types of contrast agents, are highly desirable.

Replacement Page 3, first paragraph (partial - continues from previous page),

Summary.

producing a derivatized reduced polysaccharide iron oxide complex, and sterilizing the complex by autoclaving. According to this method, producing the complex can include derivatizing a reduced polysaccharide by carboxyalkylation, for example, wherein the carboxyalkylation is a carboxymethylation. The term "derivatizing" and related terms (e.g. derivatives, derivatized, derivatization, etc) refer to the conventional sense of functionalization at the reactive sites of the composition. Further according to this method, the reduced polysaccharide can be a reduced dextran. The derivatized, reduced polysaccharide can be isolated as the sodium salt and does not contain an infrared absorption peak in the region of $1650\text{-}1800\text{ cm}^{-1}$. In one aspect of the method, producing the derivatized reduced polysaccharide is achieved at a temperature of less than approximately 50°C . In another aspect of the method, producing the derivatized reduced polysaccharide is achieved at a temperature of less than approximately 40°C . In a further aspect of the method, the iron oxide is superparamagnetic.



REMARKS

Response B, filed April 25, 2002 includes replacement paragraphs in the Version With Markings to Show Changes (see pp. 27-28 of Response B). However, no clean replacement paragraphs were provided. Therefore, Applicants herein supply the clean paragraphs, and re-supply the marked up paragraphs, for clarity.

It is believed that no extension of time is needed; however, this conditional petition for an extension of time is being made in the event that the need for an extension has been overlooked. If any additional fees are required for the timely consideration of this application, please charge deposit account number 19-4972. The Examiner is requested to telephone the undersigned if any matters remain outstanding so that they may be resolved expeditiously.

Date: June 4, 2002

Respectfully submitted,



Bruce D. Sunstein
Registration No. 27,234
Attorney for Applicants

Bromberg & Sunstein LLP
125 Summer Street
Boston, Massachusetts 02110-1618
Tel: (617) 443-9292
Fax: (617) 443-0004